



Armed Forces College of Medicine AFCM



Year 2

Endocrine and genitourinary module

Clinical Integrated Cases

Basic Science Principles for Clinical Reasoning



- 1- Critical thinking
- 2- Introduction to common forms of disease
- 3- Apply basic knowledge in a realistic clinical scenario.
- 4- Interpersonal skills-(share and apply your knowledge)

communication...patient safety

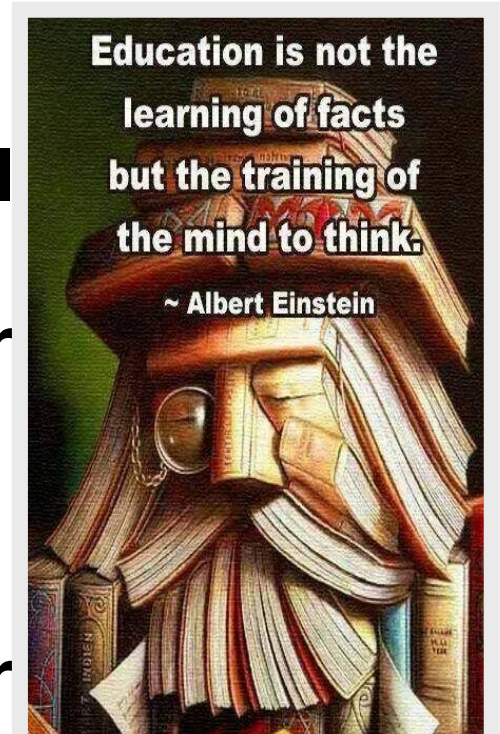
- 5- Life long self directed learning
- 6- using a concept map to take the proper decision

Doctor-patient relationship and
involving the patients in
management decision

Case co-ordinators

**Prof. Drs.
Nourhan**

Manal Hassa, Lamiaa Foad,



Sharing Departments

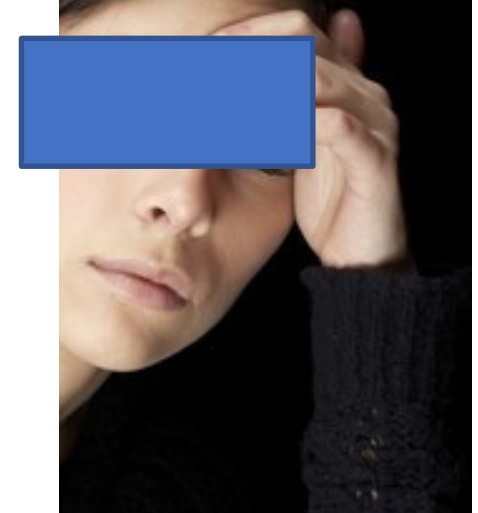
- **Internal medicine**
- **Physiology**
- **Biochemistry**
- **Pathology**
- **Histology**
- **Anatomy**
- **Pharmacology**

**I am losing
weight**

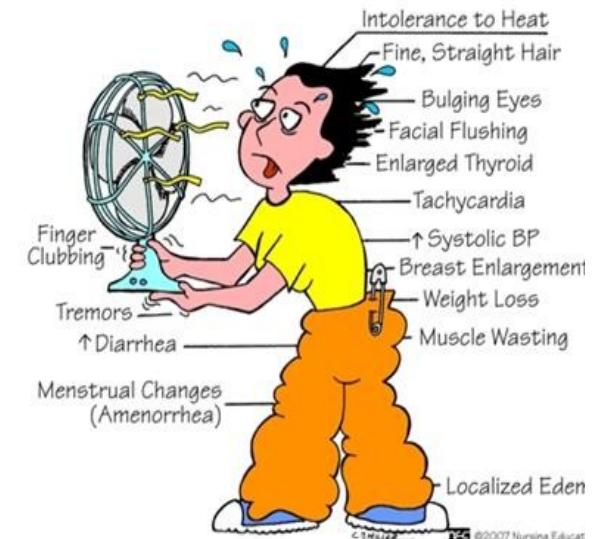
I am losing weight



Suzan is a **32** year old female, married and has 2 children. She is an accountant in a national bank.



Her husband Medhat noticed that she is **using the fan although the weather is not hot**. He also asked his wife whether she is on a diet as she is **losing weight** within the last couple of months.



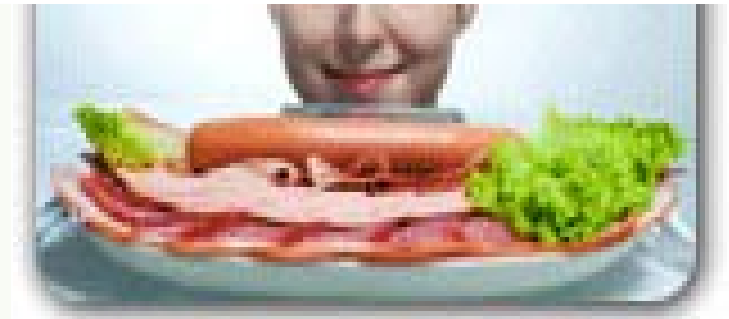
I am losing weight



Suzan was worried and decided to go to an internist. The physician started to take history from Suzan and asked her about her **appetite** and whether she is suffering from **gastrointestinal disturbance** or **polyuria**.

Suzan said that she had **good appetite** and she is losing weight despite increased appetite.

She occasionally had **diarrhea**.
She denied presence of polyuria



Feeling hungry

I am losing weight



She mentioned that she **cannot tolerate hot weather** and she was **irritable** and often shouting at her children. She also suffered from **sleeplessness**

She often **feels her heart beats**.

She complained of **irregular menstruation**.

The doctor asked her about using **contraceptive pills**. She denied **General examination:**

The doctor noticed that the patient was **sweating**.



Difficulty in sleep



I am losing weight



Vital signs

- Pulse rate was regular but was **110/minute**
- Blood pressure was **160/85mmHg**.
- Temperature: 37°C
- Respiratory rate: 16/min



Elevated blood pressure

Her height was **159 cm** and
weight was **44 Kg**.

So, BMI is....

Neck examination showed a
swelling in the front of the neck
that **moves up and down when**
he asked her to swallow.



I am losing weight



Eye examination:

Suzan had a **staring look** and **lid lag**

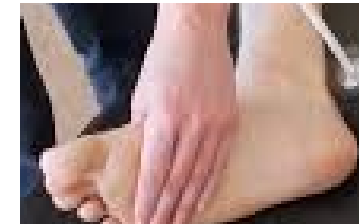


Hand examination showed **palmar erythema** and **fine tremors**.



Hand tremors

Motor examination showed **hyper-reflexia**.



Discussion

Build your concept map

1- a- List the patient problems

b- What is the differential diagnosis?



History:

Weight loss + good appetite

Diarrhea

Heat Intolerance

Irritability

Insomnia

Palpitation

Menstrual Irregularity

Examination:

Sweating

Tachycardia

Wide Pulse Pressure

Neck Swelling

Exophthalmos

Palmar Erythema

Fine Tremors

Hyper-reflexia

Differential diagnosis of losing weight inspite of good appetite

- Thyrotoxicosis
- Diabetes Mellitus
- Malabsorption syndrome
- Parasitic infestation

Causes of thyrotoxicosis:

Diffuse toxic goiter (Graves' disease)

Toxic adenoma

Toxic multinodular goiter (Plummer's disease)

Subacute thyroiditis

"Silent" thyroiditis

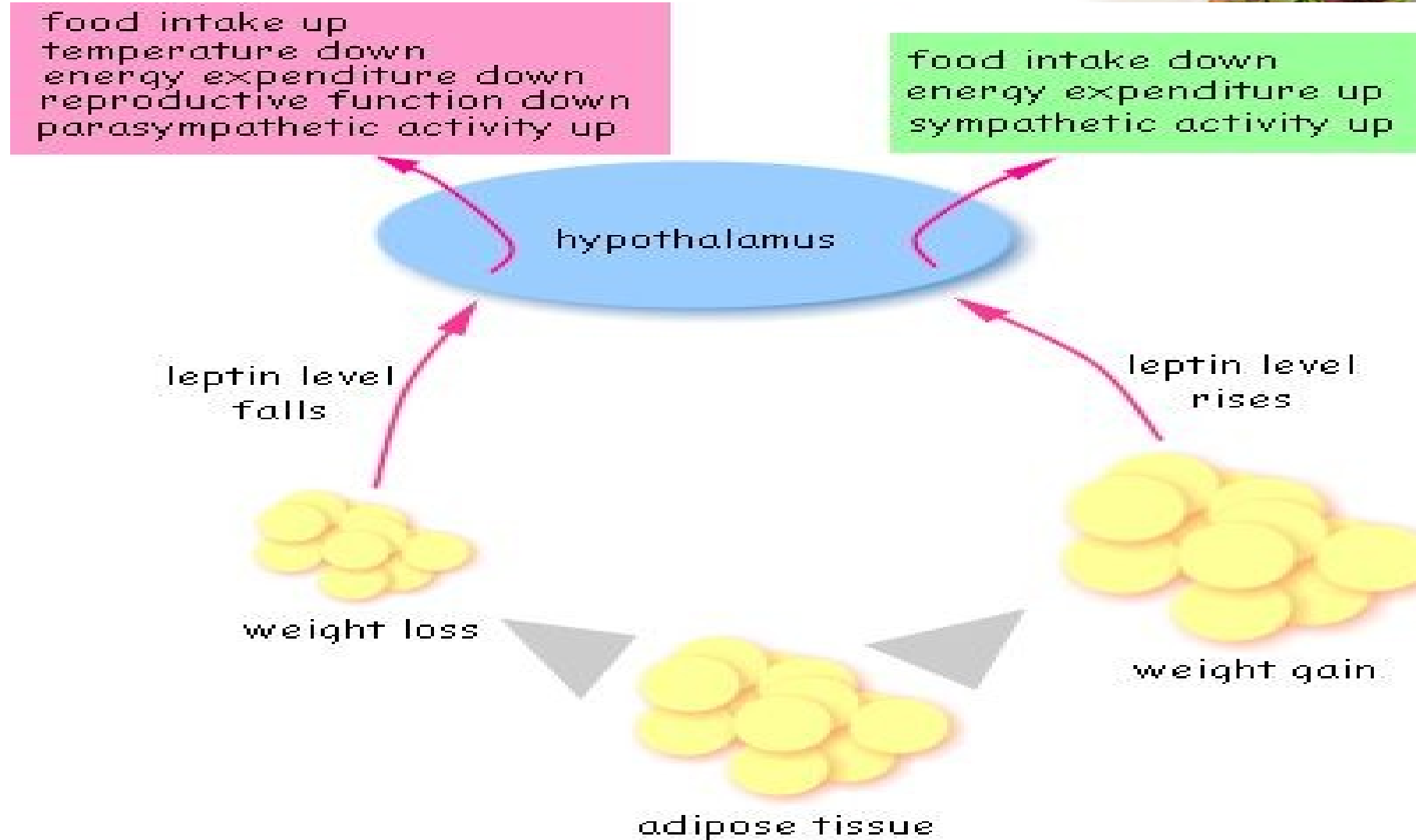
Thyrotoxicosis factitia

2- What is the mechanism of losing weight in a case of thyrotoxicosis despite increased appetite?

- **Calorigenic action**

- T4 and T3 **increase O₂ consumption** by almost all metabolically active tissues.
- Some of the calorigenic effect of thyroid hormones is due to **lipolysis** and **protein catabolism** (endogenous protein and fat stores are catabolized and weight is lost)
- Also, excess thyroxine causes **uncoupling of oxidative phosphorylation** reaction, So energy is lost as heat contributing to **weight loss**
- Decreased leptin \square **increased food intake**

Increased appetite



She occasionally had **diarrhea**.

Explain

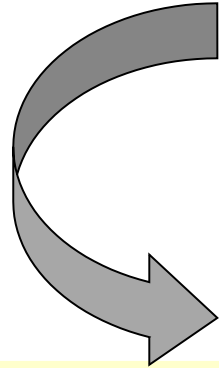
- Gastrointestinal motor dysfunction is widely accepted as the main cause of symptoms in hyperthyroidism. **Intestinal hypermotility** in thyrotoxicosis reduces small bowel transit time.
- Increased appetite and excessive **fat-rich food intake** may contribute to excessive fecal fat.
- Moreover, diarrhea may be related to a **hypersecretory** state within the intestinal mucosa.
- A reduction in mixing of food with digestive secretions may also contribute to decreased fat absorption.
- Therefore, hyperthyroidism leads to increased motility leading to diarrhea and malabsorption, while the lack of thyroxine causes

She mentioned that she **cannot tolerate
hot weather**

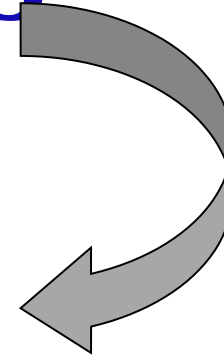
Explain

Thyroid hormone

Thyroid hormone is a major regulator of thermogenesis:



Increase metabolic rate by **uncoupling** electron transport from ATP synthesis



Increase expression and transcription of genes for uncoupling proteins

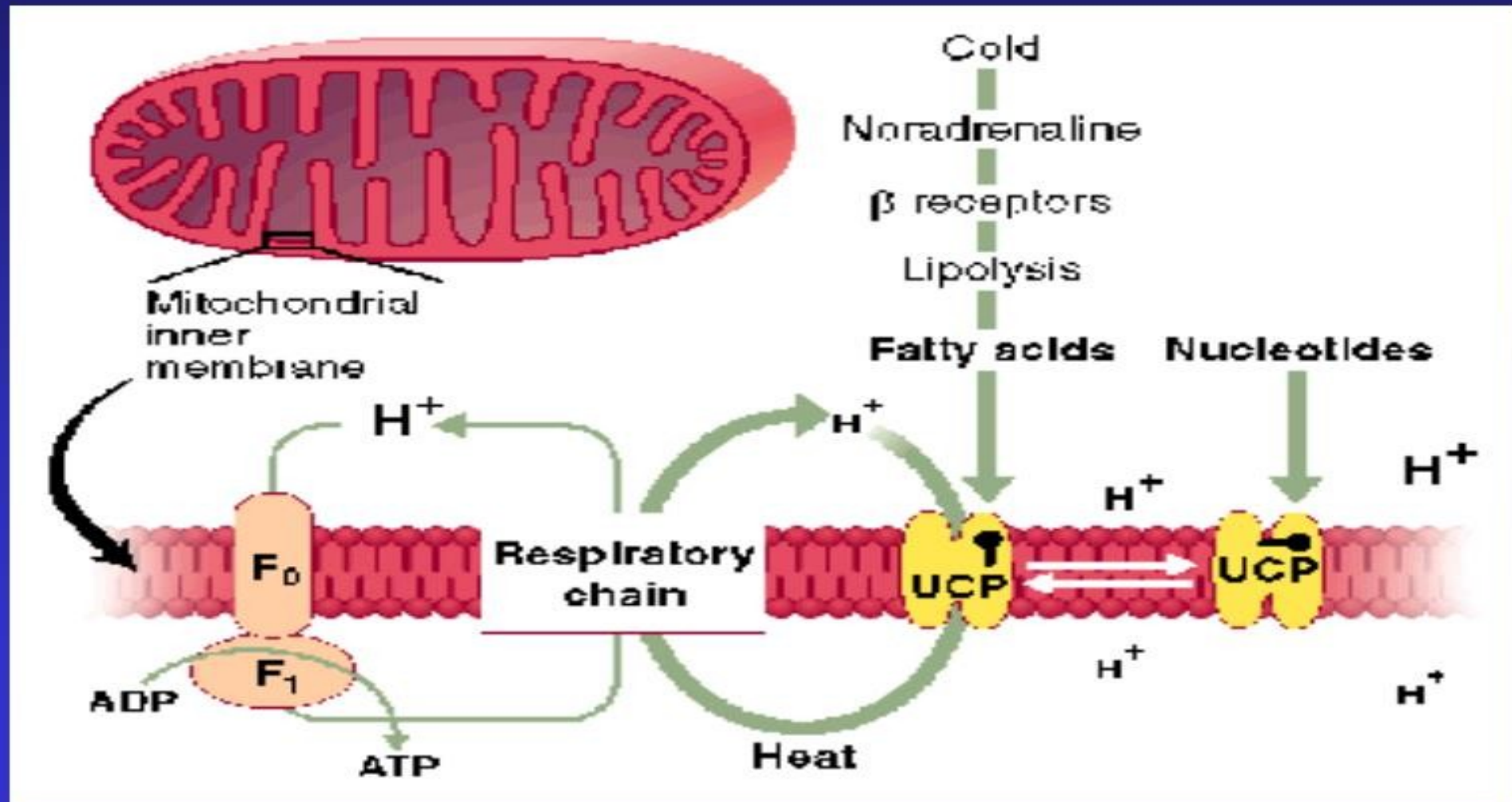
Uncoupling proteins

Present in almost **all tissues.**

Involved in the mechanisms of cellular **thermogenesis.**

Mediators of thyroid thermogenesis.

Uncoupling proteins



General examination,

- Pulse rate was regular but was

110/minute

- Blood pressure was

160/85mmHg.

3- Explain the tachycardia and wide pulse pressure

Thyroxin **increases the number and sensitivity of beta adrenergic receptors (B1)** “enhanced response to catecholamines” □ increased heart rate “tachycardia”

- Because of increase in rate and force of contraction of the heart, cardiac output increases □ increased Systolic blood pressure.
- Increased metabolism □ peripheral vasodilatation with decreased peripheral resistance □ decreased diastolic pressure.
- So, the pulse pressure increases.

Neck examination showed a swelling in the front of the neck that **moves up and down when he asked her to swallow.**

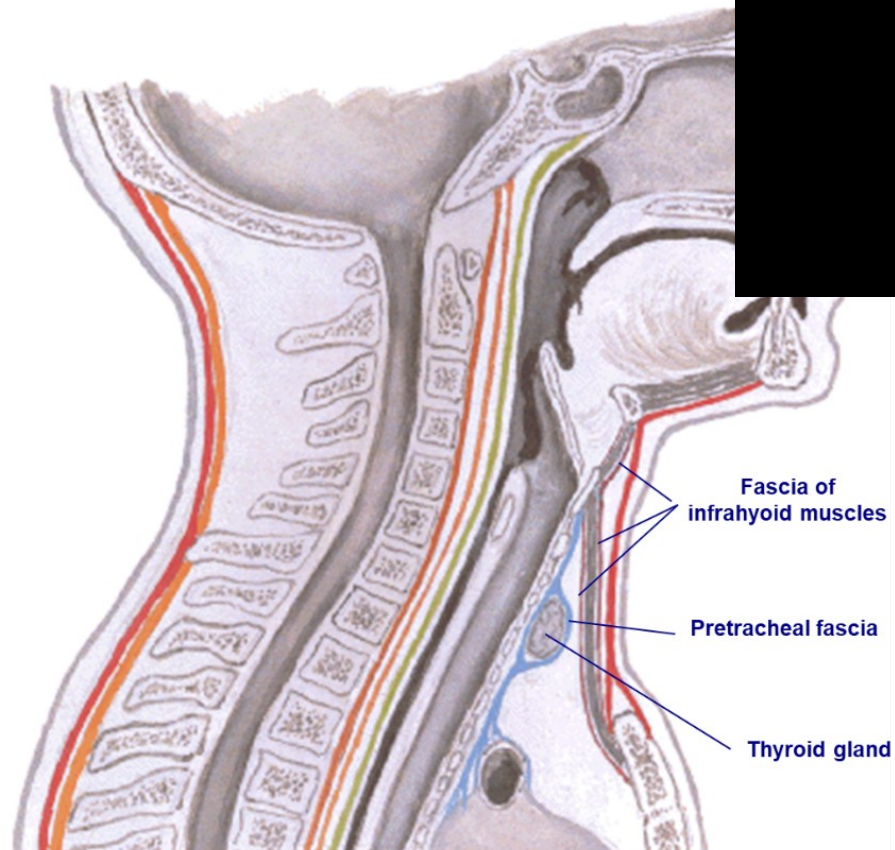


4- Explain why the swelling moves with deglutition?

- The thyroid gland is covered by the pretracheal fascia which attaches the gland to the oblique line of the thyroid cartilage, this explains movement of the thyroid gland with movement of the larynx.

Pretracheal
Fascia

Thyroid
gland



Hand examination showed palmar erythema and **fine tremors**.

Motor examination showed **hyper-reflexia**.



Interpret the palmar erythema and tremors and hyperreflexia

Palmar erythema

- Vasodilation

- An increase in cutaneous blood flow causes the warmth which often occurs along with redness of the face, elbows, and palms (palmar erythema)
- N.B. increased thyroxine \rightarrow increased BMR \rightarrow so, there is excessive sweating “to increase heat loss” + V.D of Bl.

Vs

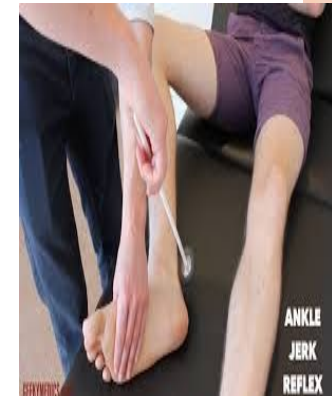
Tremor

This is due to increased responsiveness to catecholamines \rightarrow Increased reactivity of the neuronal synapses in the areas of the spinal cord that control muscle tone & increased activation of the reticular activating system \rightarrow tremors



Hyperreflexia

Thyroid hormones increase the sensitivity of stretch reflex receptors specially nuclear bag \rightarrow exaggerated response to average stretch (shortened reaction time of stretch reflex)



5- What are the investigations that should be done to Suzan?

Welcome Back

I am losing weight



The doctor asked for

- Complete blood picture,
- **Thyroid function tests (free T3, free T4, TSH)**
- **Fasting blood sugar, HBA1c**
- **ECG**
- **Stool examination**
- **Neck ultrasonography**
- **^{99m}technetium scintigraphy s**



I am losing weight

- Free serum T4 = **3.5**/dL (0.7-1.9 ng/dl)
- Free serum T3 = **250** ng/dL (80-180 ng/dl)
- Serum TSH = **0.1** μ U/ml (0.5-6 μ U/ml)
- Fasting blood sugar: **100 mg/dl**

99mTc thyroid scintigraphy scan results showed increased **diffuse uptake** by the thyroid gland.



US diffuse enlargement and high vascularity

I am losing weight



The doctor asked for **TSH- receptor antibodies**

TSH-receptor antibodies were 15.5 IU/L (1.75 IU/L)

The doctor prescribed

- **Propranolol** : 10mg 3 times daily for 6 weeks

The doctor asked her to

- **Carbimazole** 10mg 3 times daily for 6 weeks
- Follow up every 6 weeks

and told her that she must take the treatment to avoid irreversible complications as exophthalmos **permanent protrusion of her eye.**

- The doctor also advised her to contact him if she got pregnant during the treatment period.

- **Complete blood picture if she suffers sore throat.**



Discussion

- **Free** serum T4 = 3.5/dL (0.7-1.9 ng/dl)
- **Free** serum T3 = 250 ng/dL (80-180 ng/dl)
- Serum TSH= 0.1uU/ml (0.5-6 uU/ml)

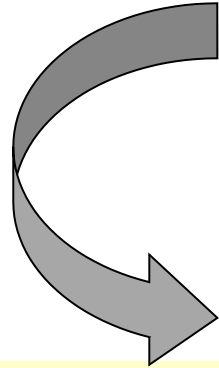
6- a-Why did the doctor ask for free thyroid hormone levels?

B- Explain the biochemical basis

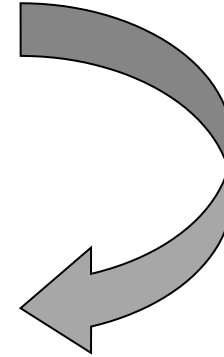
Because the free forms are not affected by thyroid binding globulin levels

Lipophylic hormones bind to Intracellular Receptors

Intracellular Receptors are :



Cytoplasmic
As Steroid
hormones
receptors



Nuclear
As thyroid
hormone
receptors

Thyroid hormone

- Thyroid hormones are highly lipophilic molecules due to the **iodinated aromatic rings**.

Present in the blood either **bound** or **unbound** to plasma proteins.

Free, unbound thyroid hormones are the only form that has **endocrine activity** as it can **freely diffuse** through cellular plasma membranes

Thyroid hormone

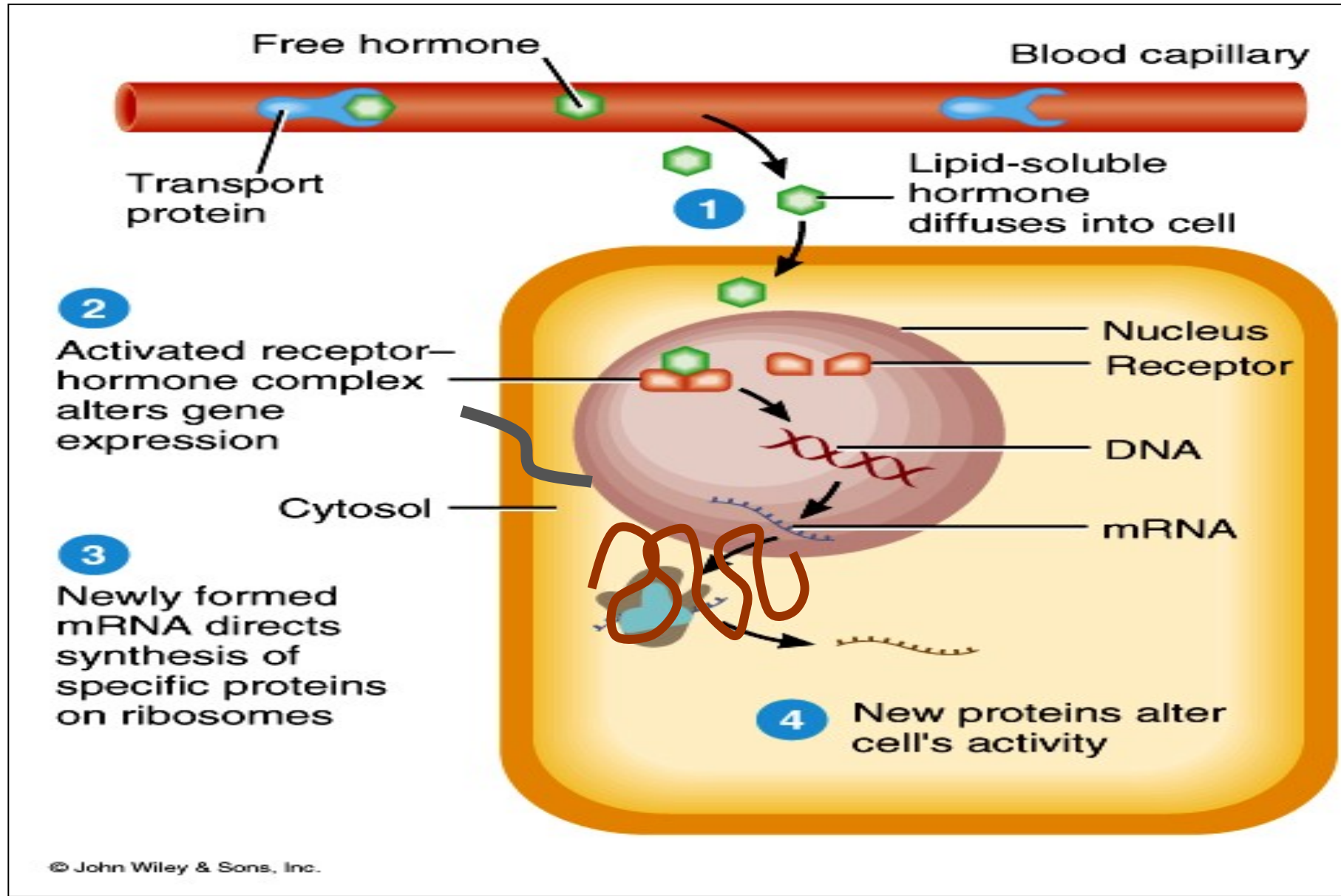
- The **majority** of thyroid hormones in the blood are **non-covalently bound** by the **plasma protein Thyroxine-binding Globulin (TBG)** produced by the liver.

The TBG-bound thyroid hormones do **not** have any **endocrine activity** because they **cannot cross** plasma membranes of cells.

TBG-bound thyroid hormone does act as a **reservoir** of the hormone in the body.

Nuclear receptors

Thyroid hormones exerts many of its effects on energy metabolism by affecting gene transcription



Explain the increase in T3 with decrease in TSH?

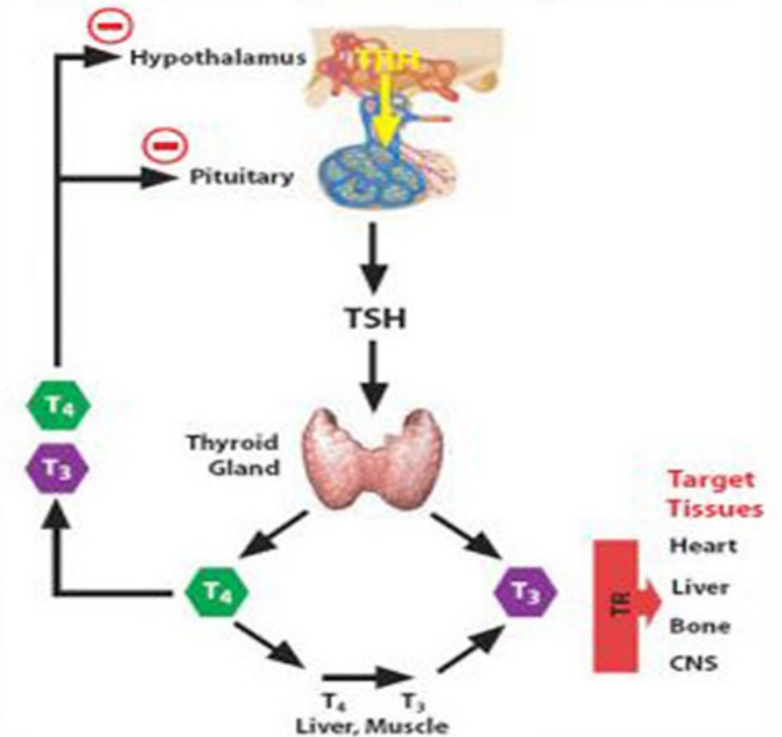
- **Thyroid-stimulating hormone (TSH)** secreted by anterior pituitary is the major factor regulating the synthesis and release of thyroid hormones. It is also necessary for the growth and the secretory activity of the thyroid gland. Thus, TSH influences every stage of formation and release of thyroid hormones
- **Thyroid hormones** regulate their own secretion through negative feedback control, by inhibiting the release of TRH from hypothalamus and TSH from anterior pituitary

Feedback effect of thyroid hormones:

The increased thyroid hormones produce:

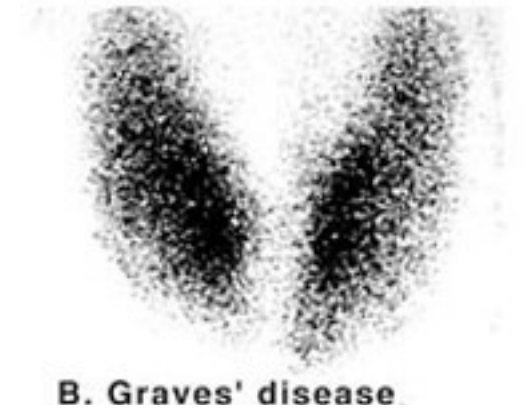
- **A direct effect of T3 & T4 on the pituitary** causing decreased production of TSH secretion.
- **Secondary weak effect on the hypothalamus** causing a decrease in TRH secretion

Hypothalamo- pituitary-Thyroid Axis

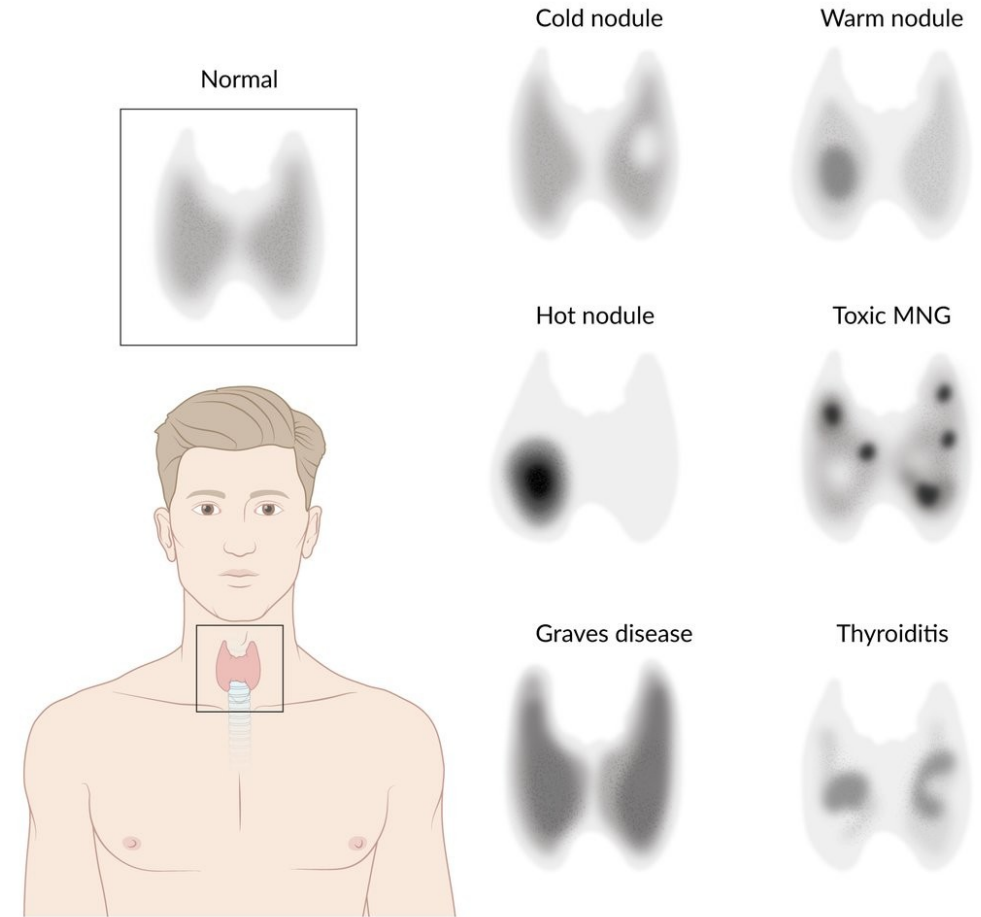


^{99m}Tc technetium scintigraphy scan results showed **diffuse uptake** by the thyroid gland.

Why ^{99m}Tc technetium scintigraphy?



Thyroid scanning shows the
different etiological causes of
hyperthyroidism



The doctor asked for **TSH- receptor antibodies**
TSH-receptor antibodies were 15.5 IU/L (1.75
IU/L)

7- Why?

Graves' disease (1ry hyperthyroidism) ***(Diffuse toxic goiter or Exopthalmic goiter)***

Pathogenesis

- ❑ Is an autoimmune disease
- ❑ Caused by group of autoantibodies

1-Thyroid stimulating immunoglobulins (TSI):most important
(act on TSH receptors mimicking the action of TSH) bind to the thyroid follicle cells and stimulate the gland to secrete T3 and T4. The rise in thyroid hormone concentration will suppress TSH secretion.

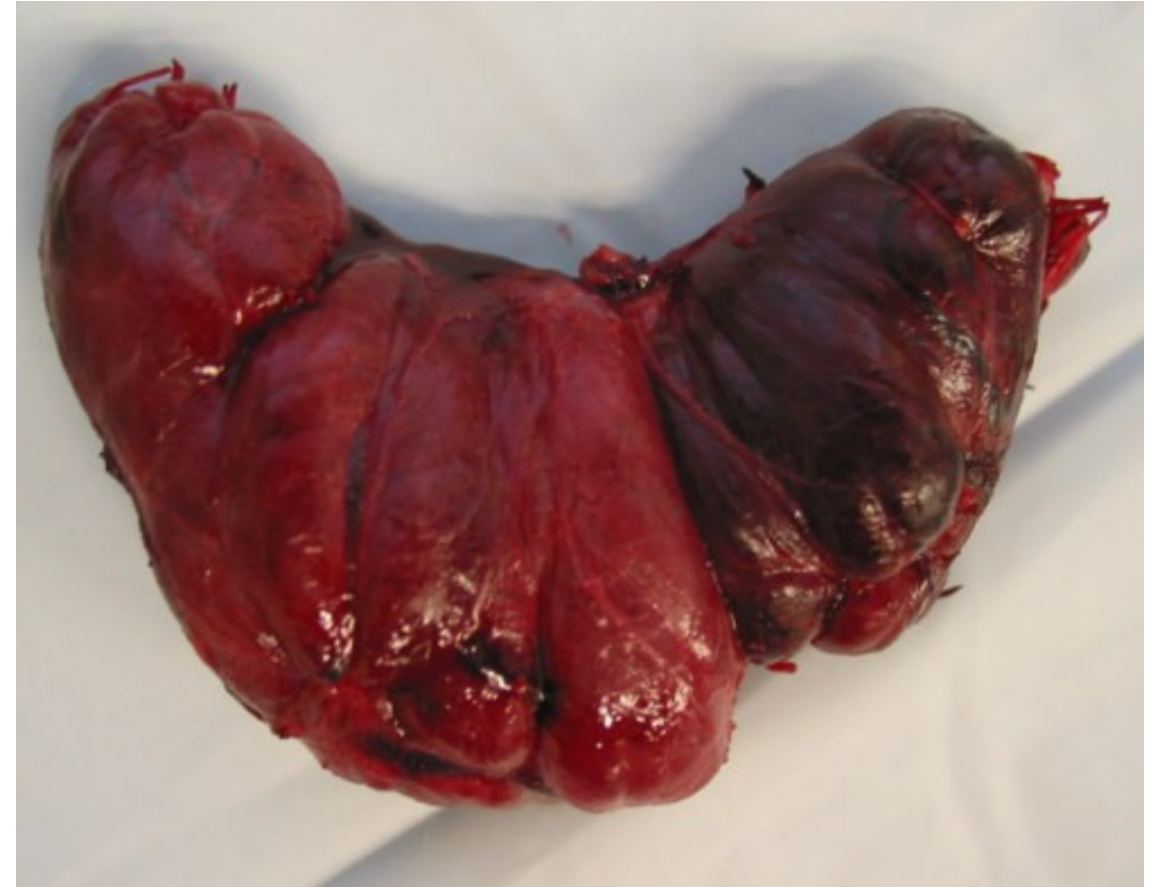
2-Thyroid growth-stimulating immunoglobulins.

Also directed against the TSH receptor,
Causing proliferation of thyroid follicular epithelium.

Explain the pathological changes that occurred in thyroid gland of Suzan?

Gross

- ❑ Moderate diffuse symmetrical thyroid enlargement
- ❑ Cut section is pink due to high vascularity



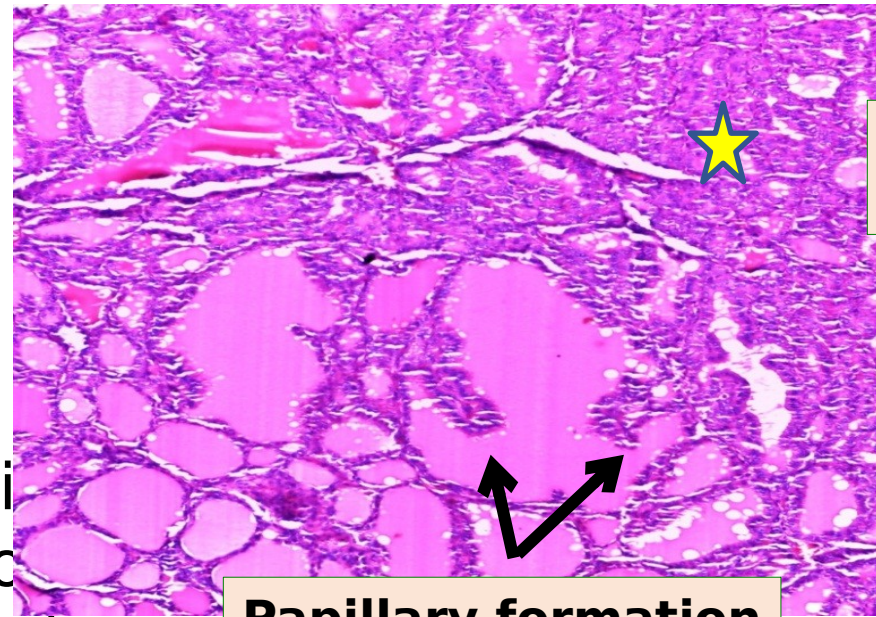
Mic:

Thyroid follicles

- ❑ Hyperplastic
- ❑ lined by columnar cells with frequent papillary formation
- ❑ The colloid is scanty which is peripherally scalloped (vacuolated) due to rapid absorption of thyroid hormones

Thyroid stroma shows

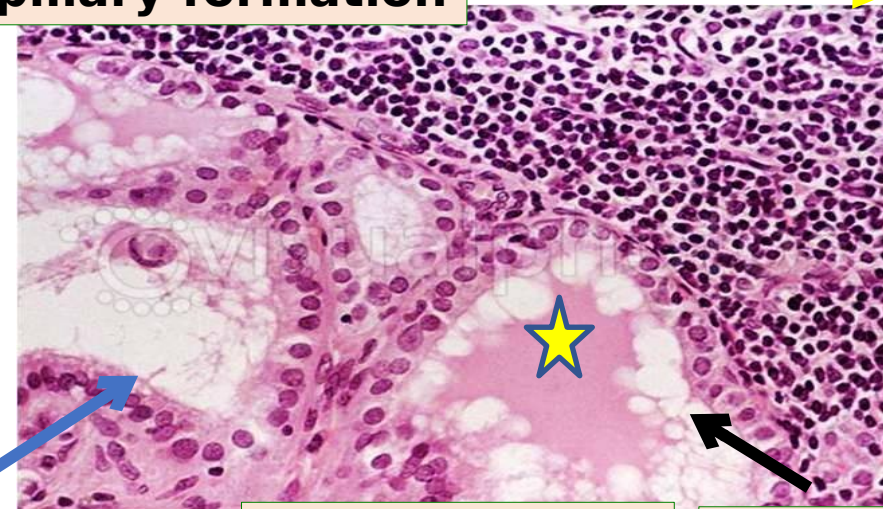
- ❑ Lymphocytic infiltration
- ❑ High vascularity



Hyperplastic thyroid follicles

Papillary formation

Lymphocytes



Scanty colloid

Peripheral scalloping

Columnar cells

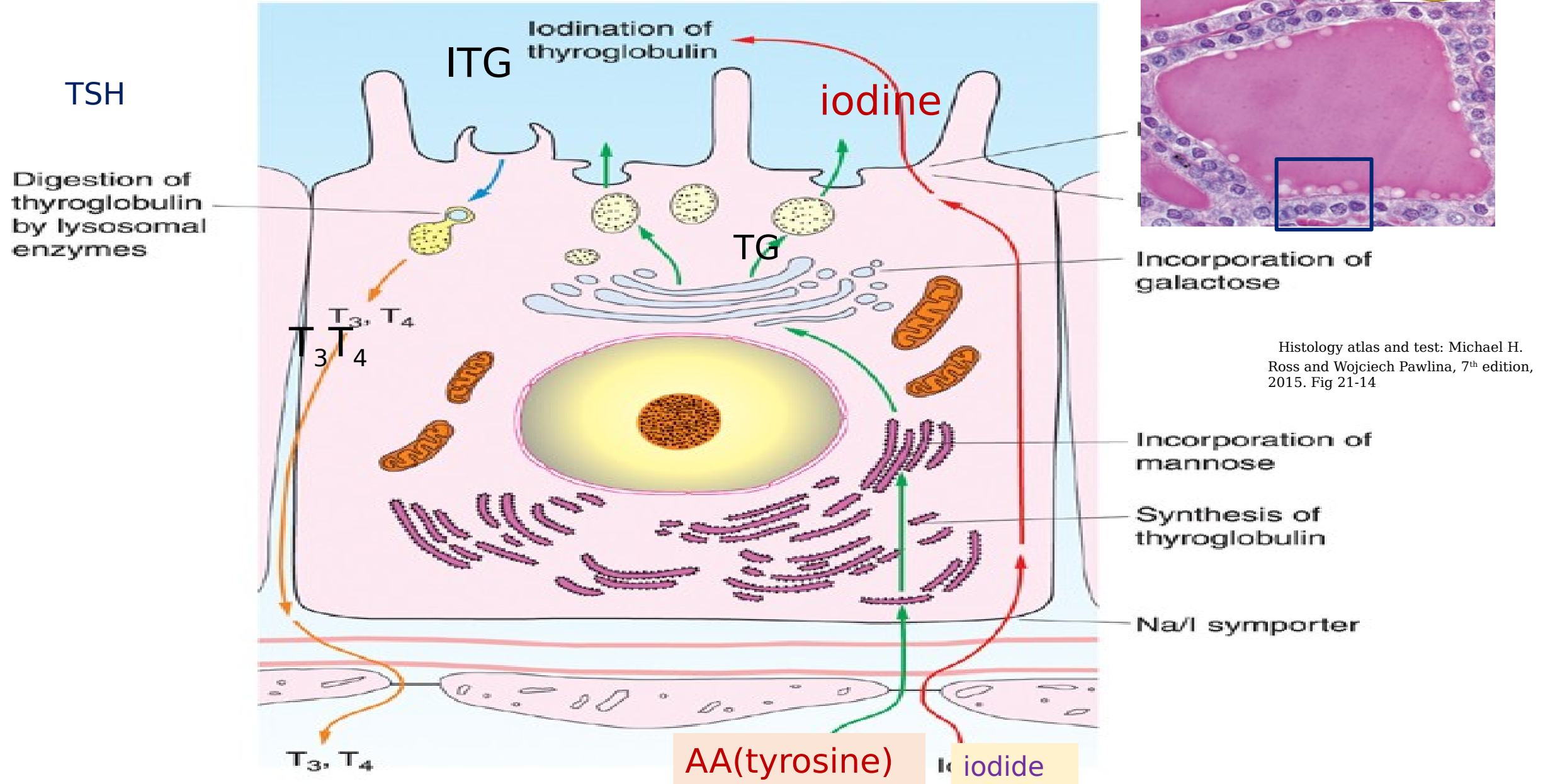
The doctor prescribed

- **Propranolol**
- **Carbimazole** to decrease thyroid hormone synthesis.

8- Why propranolol ?

- **Control CVS symptoms**
- **Prevent conversion of T_4 to T_3**

Thyrocyte organelles



The doctor prescribed

- **Propranolol**
- **Carbimazole** to decrease thyroid hormone synthesis.

9- Why carbimazole?

What is the mechanism of action?

Mention its side effects

Why carbimazole?

Inhibit synthesis of thyroid hormones

What is the mechanism of carbimazole?

- **Inhibition of oxidation of iodide to iodine.**
- **inhibit the iodination of tyrosine**
- **inhibit coupling of iodotyrosines to form T₃ and T₄**

What are the Adverse effects of carbimazole?

Most common: rash

Most dangerous but Rare & reversible: agranulocytosis
cholestatic jaundice

Loss of hair, abnormal hair pigmentation

10- What if she became pregnant?

Propylthiouracil is used in the **first trimester** of pregnancy **instead of carbimazole**, as carbimazole is teratogenic causing fetal goiter.

Then **after the first trimester**, shift again to **carbimazole**

The doctor asked her to **follow up** every 6 weeks

The doctor advised her **not to get pregnant** during the treatment period.

Complete blood picture if she suffers sore-throat.

How could you monitor the patient?

Clinically

Clinically: improvement of symptoms and signs

Laboratory

Laboratory: normal FT4 and TSH

Welcome Back

I am losing weight



After treatment for 18 months, the patient improved

But

relapse occurred with reappearance of the symptoms 6 months after cessation of therapy

The doctor discussed with Suzan the

other different treatment modalities including the use of

- **Radio-active iodine** and
- **Near total Thyroidectomy**



I am losing weight



Suzan was **anxious** from the possibility of doing an operation and told her doctor that she heard about **voice problems** occurred after this procedure. The doctor re-assured her and told her that the **operation is better** than radioactive iodine for her age.



Suzan went to another physician who told her that use of **radioactive iodine is better** for her.



After treatment for 18 months, the patient improved

But

relapse occurred with reappearance of the symptoms 6 months after cessation of the drug.

How to manage relapse?

Ablation of the thyroid gland with radioactive iodine

Destroys thyroid cells.

Functioning tissue reduced beyond critical level

Accurate dosage is difficult and may require further dose after 12 weeks.

No evidence proven – therapeutic dosage is carcinogenic



Surgical : Thyroidectomy



What is better for Suzan Surgery or radioactive iodine?

Factors influencing the choice of therapy

- Type of thyrotoxicosis
- Age of the patient
- Co existing medical illness
- Post treatment care
- Follow up
- Compliance
- Patient wishes

The accepted absolute indications for surgery include:

- **Large goiter with Graves' and compressive symptoms**
- **Pregnancy or planning for pregnancy**
- **Young age**
- **Relapse after medical treatment**
- **Severe Graves' ophthalmopathy**
- **Suspicion of malignancy**
- **Patient's preference.**

Indications and contraindications for RAI therapy

The main indications for RAI therapy include the following conditions

- Hyperthyroidism due to: Grave's disease,
- Toxic multinodular goiter or Hyperfunctioning thyroid nodules
- Thyroid cancer.

Contra-indications for RAI therapy:
Pregnancy

11- What are the precautions that should be taken during thyroidectomy?

How to avoid voice complications of surgery?

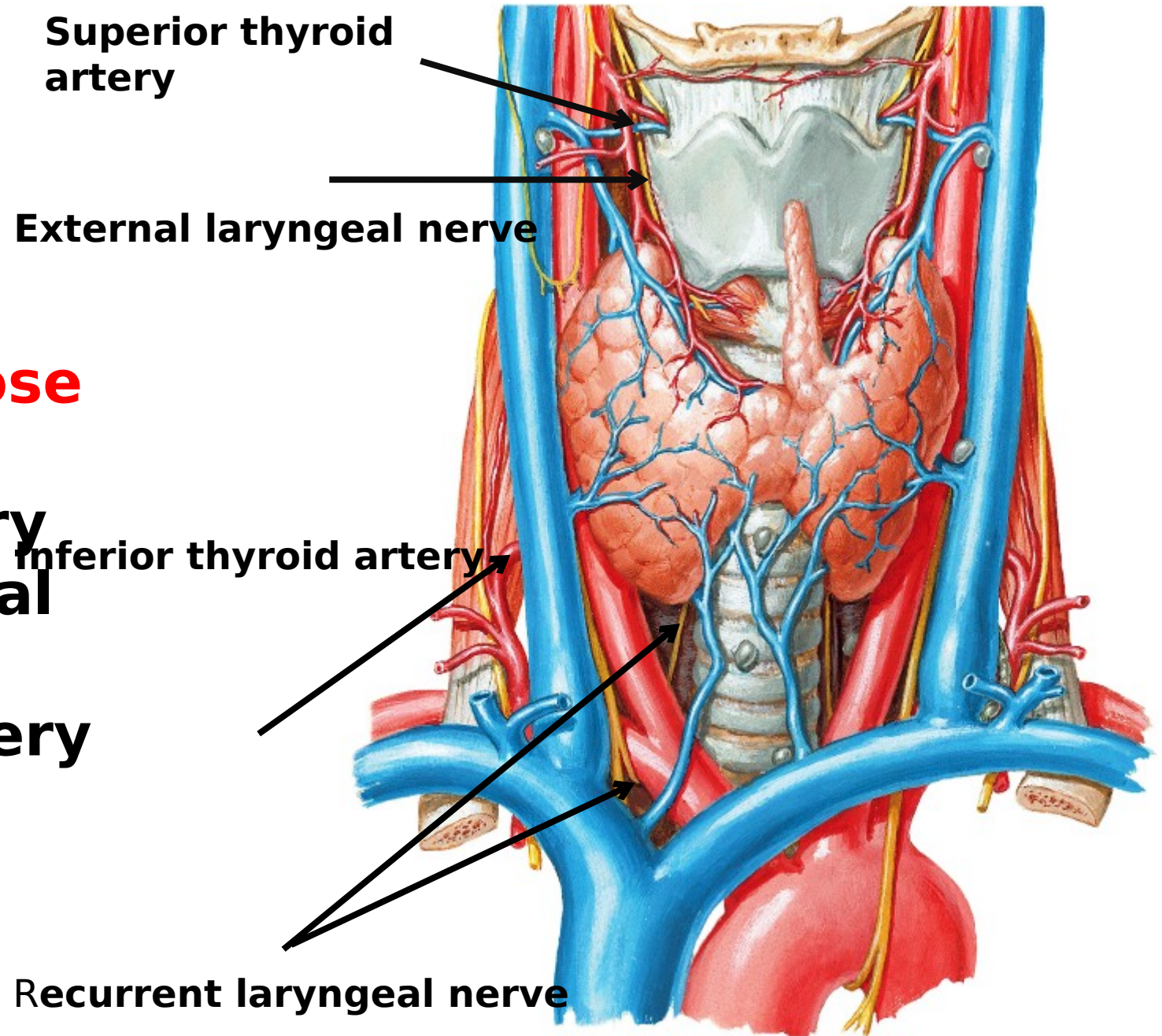
The precautions that should be taken during thyroidectomy are:

1. Avoid **injury** of **external laryngeal** and **recurrent laryngeal** nerves by **ligating**:
 - Superior thyroid artery **close** to the apex of the gland to avoid injury of external laryngeal nerve.
 - Inferior thyroid artery **away** to avoid injury of recurrent laryngeal nerve.
2. Avoid **removal** of the posterior part of each lobe to avoid **removal of the parathyroid glands** in subtotal thyroidectomy.

- **To avoid voice complications of surgery:**

- Superior thyroid artery is ligated **close** to the apex of the gland to avoid injury of external laryngeal nerve.

- Inferior thyroid artery is ligated **away** to avoid injury of recurrent laryngeal nerve.





Take home message

*Thank
you*

